Research Article

AL- ANBAR JOURNAL OF VETERINARY SCIENCES

Vol. 13 Issue:2, (2020) ISSN: P-1999:6527 E-2707:0603

Ameliorative Effect of Ethanolic Extract of *Petroselinum Crispum* Against Gentamicin-Induced Nephrotoxicity in Rabbits Male

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Doi: https://doi.org/10.37940/AJVS.2020.13.2.5

Received: 2/7/2020 Accepted:6/11/2020

Abstract

The experiment was conducted to investigate the protective effect of *Petroselinum crispum* leave extracted against gentamicin-induced nephrotoxicity in male rabbits by studying the body weight, clinical signs, haematological and biochemical parameters, gross lesion and histopathological changes. Twenty four rabbits male were used and divided into 4 groups. Group 1: rabbits served as a negative control, received distilled water 1 ml(orally). Group 2: rabbits served as a positive control group, received gentamicin at a dose of 80 mg/kg/day intramuscular for 15 days. Group 3: rabbits received gentamicin at a dose of 80 mg/kg/day then after one hour treated with ethanolic extract of *Petroselinum crispum* at dose 125 mg/kg orally for 15 days. Group 4: rabbits received gentamicin at a dose of 80 mg/kg/day then after one hour treated with ethanolic extract of *Petroselinum crispum* at dose 250 mg/kg orally for 15 days.The results of the gentamicin treated group(positive control group) showed clinical signs such as loss of body weight, loss of appetite and rough hair with hematuria. The body weight a significantly declined ($p \leq 0.05$) compared other groups. There was a significant decrease ($p \leq 0.05$) in WBC count, lymphocyte, GSH, SOD, CAT, and GPX levels, while it recorded a significant increase ($p \leq 0.05$) in weights of the kidneys, neutrophils, creatinine, urea, and MDA. Histological studies showed several kidney pathological changes such as pale colour, enlargement in size and weight and easy from detaching as opposed to negative control group. On the other hand, the group treated with ethanolic extract of *Petroselinum crispum* at dose 125 mg/kg induced improved of parameters as recorded significant increased($P \leq 0.05$) in body weight, WBC count, lymphocyte, GSH, SOD, CAT, and GPX, while significant decreased ($P \leq 0.05$) in weights of the kidneys, neutrophils, creatinine, urea, and MDA compared with the positive control group whereas rabbits treated with ethanolic extract of *Petroselinum crispum* at dose 250 mg/kg restored the parameters and histological changes of the kidney to near normal status compared with the negative control group. These results showed that the dose-detected *Petroselinum crispum* extract (250mg / kg) acts as potential curative effect against gentamicin-induced nephrotoxicity in male rabbits.

Keywards: *Petroselinum crispum*, Gentamicin, Kidney, Rabbit

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تقليل تاثير لمستخلص الإيثانولي لنبات المقدونس *Petroselinum crispum* ضد السمية الكلوية التي يسببها الجنتاميسين في ذكور الارانب

الخلاصة

تم إجراء التجربة لاستقصاء التأثيرات الحماية للمقدونس ضد التسمم الكلوي الناجم عن الجنتاميسين في ذكور الأرانب من خلال دراسة وزن الجسم والعلامات السريرية والمعايير الدمية والكيميوحيوية والآفات العيانية والتغيرات النسجية.تضمنت الدراسة استخدام 24 ارنب ، قسمت الأرانب إلى 4 مجموعات , 6 ارانب لكل مجموعة ، المجموعة 1: مجموعة السيطرة السالبة, أرانب سليمة جرعت 1 مل من الماء المقطر. المجموعة 2: مجموعة السيطرة الموجبة ، ارانب حقنت بالجنتاميسين عضليا بجرعة 80 ملغم / كغم / يوميا لمدة 15 يوما. المجموعة 3: حقنت الأرانب بالجنتاميسين عضليا بجرعة 80 ملغم / كغم / يوميا ثم بعد ساعة عولجت بالمستخلص الايثانولي للمقدونس بجرعة 125 ملغم / كغم عن طريق الفم لمدة 15 يومًا. المجموعة 4: حقنت الأرانب بالجنتاميسين عضليا بجرعة 80 ملغم / كغم / يوميا ثم بعد ساعة عولجت بالمستخلص الايثانولي للمقدونس بجرعة 250 ملغم / كغم عن طريق الفم لمدة 15 يومًا.
أظهرت نتائج المجموعة المعالجة بالجنتاميسين (مجموعة السيطرة الموجبة) علامات سريرية مثل فقدان وزن الجسم وفقدان الشهية والشعر الخشن مع بيلة دموية. . انخفاض معنوي ($p\leq 0.05$) في أوزان الجسم للأرانب مقارنةً مع المجموعات الأخرى, كذلك كان هناك انخفاض كبير ($p\leq 0.05$) في عدد خلايا الدم البيضاء ، الخلايا الليمفاوية ، GSH، SOD، CAT و GPX ، بينما سجلت الدراسة وجود زيادة معنوية ($p\leq 0.05$) في أوزان الكلى ، العدلات ، الكرياتينين ، اليوريا و MDA. أظهرت الدراسة النسجية العديد من التغيرات المرضية في الكلى على عكس مجموعة السيطرة السالبة. من ناحية أخرى عندما عولجت الارانب في المجموعة الثالثة بالمستخلص الإيثانولي للمقدونس بجرعة 125 ملغم / كغم أدى إلى حدوث تحسن معنوي ($p\leq 0.05$) في بعض المعايير مثل وزن الجسم ، عدد خلايا الدم البيضاء ، الخلايا الليمفاوية ، GSH، SOD، CAT ، و GPX ، وانخفاض معنوي ($P \leq 0.05$) في أوزان الكلى ، العدلات ، الكرياتينين ، اليوريا ، و MDA مقارنة مع مجموعة السيطرة الموجبة في حين أن الأرانب المعالجة بالمستخلص إيثانولي للمقدونس بجرعة 250 ملغم / كغم لوحظ عدم وجود فروقات معنوية مقارنة مع مجموعة السيطرة السالبة بسبب اقتراب المعايير اعلاه من القييم الطبيعية لمجموعة السيطرة. كشفت هذه النتائج أن مستخلص المقدونس بجرعة(250ملغم / كغم) يعمل كمضاد للأكسدة وله تاثير علاجي قوي ضد السمية الكلوية التي يسببها الجنتاميسين في الأرانب وهذا يعود الى المركبات الفعالة الموجودة في النبات والتي تشمل مركبات الفلافونويد والأبيجينين والقلويدات والتانينات والراتنجات والبروتينات والصابونين.

Introduction

From ancient times medicinal plants, also known as medicinal herbs, have been discovered and used in conventional medical practices. Parsley *(Petroselinum crispum)*, of the *Apiaceae* family, is a culinary herb widely used in many countries to spice food. Phytochemical analysis of Parsley confirmed that several classes of flavonoids are present. In nature, flavonols (quercetin and kaempferol) and flavones (apigenin and luteolin)(1). This includes many vitamins including A, B, E, C, K, beta-carotene, manganese, iron, magnesium, potassium, sulphur, phosphorus, and sodium(2). Parsley is historically used for menstrual disease, emmenagogue, galactagogue, intestinal cramps, hepatoprotective, brain-protective, antidiabetic, analgesic, diarrhea and in contrast to the operation of the head lice, anti-cancer, and spasmolytic (3). Along with being useful for the antiplatelet, anti-anaemic, menorrhagia, anti-coagulant, anti-hyperlipidemic, anti-hypertensive, anti-inflammatory effects. *Petroselinum crispum* also alleviates an asthma-like allergy, gastroprotective, cytoprotective, laxative, estrogenic, diuretic, chronic bronchitis, dyspepsia, Alzheimer's disease, Kidney stones with thrombosis, prostatitis, cramps, indigestion, anorexia, inflammation, rheumatism and strokes (4),(5).

Gentamicin is a protein synthesis inhibitor antibiotics that belong to the aminoglycoside group used to treat various bacterial infections by binding to the bacterial ribosome subunit of the 30s. Unfortunately, 30 % of GM-treated patients had signs of toxicity and nephrotoxicity over 7 days (6). The nephrotoxicity of gentamicin caused by retention in proximal tubular cells is prevented by calcium-mediated transportation pathways. This results in kidney damage, ranging from mild, reversible renal impairment to serious acute tubular necrosis, potentially

irreversible.(7). Chronic or elevated doses of gentamicin cause in vitro and in vivo, radical development and oxidative stress induction. Gentamicin activates superoxide anions of the mitochondrial anion that contain hydrogen peroxide and hydroxyl radicals. Gentamicin also stimulates the respiratory chain of mitochondria for generations of free radicals (8). A complication common to many medicines and Elements for diagnosis is the nephrotoxicity induced by the drug. Symptoms of drug-induced nephrotoxicity include acid-base abnormalities, urinary sediment irregularities, proteinuria, pyuria, electrolyte imbalances, hematuria, and, most commonly, a drop in glomerular filtration levels. Drug-induced nephrotoxicity mechanisms that vary between different groups of drugs or products and are usually classified according to the histological portion of the affected kidney (9). This research was planned to investigate the effect of Petroselinum crispum ethanolic extract on the nephrotoxicity induced by gentamicin in male rabbits.

Material and methods

Preparations of the Ethanolic extract of *Petroselinum crispum:*

Parsley(Petroselinum crispum) leaves was obtained from the local market (Iraq-Basrah-town market), washed with distilled water and then dried out 25 ° C. Then, The ground material was obtained by grinding dry parsley flakes with a coffee grinder and the standard sieve number 20 to the powdered material and stored at room temperature.250 millilitres of (70 %) absolute ethanol were added to 50 gm of *Petroselinum crispum* powder to obtain hot alcohol extraction at 60 °C. The solution left in reflux for 3 days by Soxhlet then filtered by Whatman No. 3 and evaporated by rotary evaporator at 60 °C(10).

Experimental designs:

In the animal house of College of Veterinary Medicine/ Basra University. Twenty four male rabbits used , their weight ranged between (1300-1500 g) and aged between 8-9 months, They were divided into 4 groups (6 rabbits per group). each group was treated for 15 days as follows:

Group I: rabbits were served as a negative control group and received orally distilled water (1 ml/kg).

Group II: rabbits were served as a positive control group and received gentamicin (gentamicin form the veterinary pharmacy – United veterinary drugs industrial CO. LTD) at a dose of 80 mg/kg/day intramuscular injection(11).

Group III: rabbits received gentamicin at a dose of 80 mg/kg/day IM then after one hour orally treated with ethanolic extract of *Petroselinum crispum* at dose 125 mg/kg .

Group IV: received gentamicin at a dose of 80 mg/kg/day IM then after one hour orally treated with ethanolic extract of *Petroselinum crispum* at dose 250 mg/kg (12)**.**

studying parameters:

Measuring the Bodyweight of rabbits :

The weights of each animal were recorded on zero days (pretreatment) and at the end of the experiment by using a mechanical balance (5 kg).

Clinical signs and morphological study:

Animals were routinely tracked to detect and record any changes in behaviour, anxiety, food intake and signs of trouble breathing, salivation, vomiting, muscle fatigue and any symptoms of toxicity and mortality.

Specimens collection:

1.Blood Collection:

Blood samples were collect at the end of the experiment using 10cc disposable syringe by cardiac puncture. 2ml of blood was poured into tubes containing anti-coagulants which were then used for haematological tests such as WBC, neutrophils and lymphocytes and the remainder (8ml) were poured into plane tubes to be centrifuged at (3000 rpm for 15 minutes) to get the serum which at that point moved into various

Eppendorf cylinders (13)to use in examinations of various parameters and put away at - 4 C°until used for biochemical analysis(like CAT, GPx, SOD, GSH, MDA, creatinine and urea).

2.Organs :

The kidney was removed and weighted with an electronic balance. The organs were set for histological inspection using 10 per cent of formalin.

Biochemical measurement:

1. Measurements of Malondialdehyde (MDA)

The concentration of MDA in serum was determined according to Buege and Aust method(14).

2. Measurements of superoxidase dismutase (SOD): (Hydroxylamine Method),

was analyzed by colorimetric methods using reagent kits obtained from Elabscience/ USA.

3. Measurements of Serum GSH concentration:

The serum thiol concentration was measured according to the Ellman method as follows(15)**.**

4. Measurements of Catalase (CAT):

was analyzed by using colorimetric methods using reagent kits obtained from Elabscience/ USA.

5. Measurements of Glutathione Peroxidase (GPX):

was analyzed by using colorimetric methods of reagent kits obtained from Elabscience/ USA.

6. Serum urea measurement :

Use of urea level has been estimated a commercial kit (Biolabs, France),(16).

7. Serum creatinine measurement :

Serum Creatinine was measured enzymatically by used a special chemical kit (Biolabo, France),(17).

The Histological Study:

The rabbits had been sacrificed and organ samples taken at the end of the experiment is the kidney. The organ was fixed in formalin buffered at 10 per cent, progressively dehydrated, handled with xylene and incorporated in paraffin at increased ethanol levels. Five microns thickness sections of paraffin-embedded tissue were mounted on glass slides and stained with hematoxylin and eosin stain(18).

Statistical analysis

Data obtained from the experiments were expressed as mean ± standard deviation, the results were statistically analyzed by SPSS using ANOVA and considered significant programming differences at $p \leq 0.05$(19).

Results and discussion

Clinical signs :

Rabbits treated for fifteen days with 80 mg / kg of intramuscular gentamicin daily. Rabbits displayed symptoms of lack of appetite, reduced body weight, hair loss and roughness, depression and reduced movement. In the last four days even, hematuria has been observed.

Effect of *Petroselinum crispum* extract on Bodyweight and kidneys weight in male rabbits treated with Gentamicin:

The results of the table (1) showed that the bodyweight of the positive control group had declined significantly ($p \leq 0.05$) compared to the negative group. In male rabbits treated with *Petroselinum crispum* ethanolic extract at a dose (125 mg/kg) body weight was significantly increased ($p \leq 0.05$) when against the positive control group, but still significantly lower than in the negative control group ($p \leq 0.05$). However non-significant changes($p > 0.05$) were recorded in bodyweight of rabbit treated with extract of *Petroselinum crispum* at dose(250mg/kg b.w) and negative control group.

As illustrated in the table (1) a significant weight of kidneys increase ($P \leq 0.05$) were recorded in the positive group compared with the negative group. Also, there was no significant

difference in the weight of the kidneys in male rabbits treated with *Petroselinum crispum* extract at a dose (250 mg/kg b.w) compared with the negative control group. A significant decline in the weight of kidneys were observed in male rabbits treated with *Petroselinum crispum* at a dose(125 mg/kg)compared with the positive control group but remained significantly higher ($P \leq 0.05$) than those of negative control group.

Table 1 The effect of *Petroselinum crispum* extract on body weight and kidney weight of male Gentamicin-treated male rabbits:

Groups	Initials body weight (g)	Final body weight (g)	Kidney weight (g)
control group	1200.0±379.47 a	1260.0±278.90 a	6.00±0.00 c
Gentamicin (80mg/kg)	1208.3±341.19 a	700.0±154.91 c	13.75±0.41 a
Gentamicin (80mg/kg)+PCE(125mg/kg)	1201.7±143.02 a	967.3±86.62 b	10.08±1.28 b
Gentamicin (80mg/kg)+ PCE(250mg/kg)	1203.3±342.96 a	1255.3±288.89 a	6.78±0.63 c

Different letters mean significant differences ($P \leq 0.05$) .

Effect of *Petroselinum crispum* extract on WBC count, lymphocyte and neutrophil in male rabbits treated with Gentamicin:

The effect of gentamicin was obvious on the WBC count, lymphocyte and neutrophils, where it caused a significant low($p \leq 0.05$) in the WBC and lymphocyte of The positive group is shown in the table in comparison to the negative group and another group (table 2). While the results showed non-significant changes ($p > 0.05$) in WBC count and lymphocyte in male rabbits treated with ethanolic extract of *Petroselinum crispum* at dose (250mg/kg b.w) and negative control group but the findings showed a significant increase ($p \leq 0.05$) in the rabbit treated with *Petroselinum crispum* at a dose (125mg/kg b.w) compared with the positive control group, but remain significantly lower($p \leq 0.05$) compared with the negative control group.

Result of the neutrophils showed a significant increase ($p \leq 0.05$) in the positive control group compared with the negative control group so showed a significant reduced($p \leq 0.05$)in neutrophils in male rabbits treated with *Petroselinum crispum* at a dose (125mg/kg b.w) compare with the positive control group, but showed non- a significant difference in male rabbits treated with *Petroselinum crispum* at a dose(250 mg/kg b.w)compared with the negative group.

Table 2 effect of *Petroselinum crispum* extract on WBC count, lymphocyte and neutrophil in male rabbits treated with Gentamicin:

Groups	WBC10^3/μ*l*	Lymphocyte %	Neutrophil %
control group	6.36±1.99 a	66.88±6.81 a	30.03±2.32 c
Gentamicin (80mg/kg)	3.00±0.31 c	42.41±11.97 c	48.85±9.32 a
Gentamicin (80mg/kg) +PCE(125mg/kg)	4.36±0.70 b	51.16±3.76 b	40.73±1.63 b
Gentamicin (80mg/kg)+PCE(250mg/kg)	5.83±0.45 a	60.58±2.24 a	31.16±3.04 c

Different letters mean significant differences (P≤0.05) .

Effect of *Petroselinum crispum* ethanolic extract on serum concentrations of antioxidant enzymes in Gentamicin treated male rabbits:

Table (3) shows that MDA serum concentration was significantly increasing (p≤0.05) in the positive control group compared to negative control, whereas in rabbits treated with *Petroselinum crispum* ethanolic extract at a dose (125 mg / kg b.w) was significantly reduced (p≤0.05), compared to the positive control group. onthe other hand non-significant differences (p>0.05) in MDA level between the group of ethanolic extract of *Petroselinum crispum* at dose (250 mg /kg b.w) and negative control group. A significant decline (p≤ 0.05) in serum levels of SOD, GSH, CAT and GPX enzymes in the positive control group compared with the negative group, but the results showed non-significant changes in the level of SOD, GSH, CAT and GPX in male rabbits treated with ethanolic extract of *Petroselinum crispum* at dose (250 mg /kg b.w) and negative group.

A significant increase (p≤ 0.05) in SOD, GSH, CAT and GPX enzyme was recorded in the group of *Petroselinum crispum* at the dose (125 mg/kg b.w) compared with the positive control group, but it is still significantly lower than the control group.

Effect of ethanolic extract of *Petroselinum crispum* on serum Urea and Creatinine in male rabbits treated with Gentamicin:

Table (4) shows that the gentamicin treatment resulted in a significant high(p≤ 0.05) in the serum concentrations of male rabbits in the positive control group as comparision with the negative control group and other treated group, but that there was a marked decrease (p≤ 0.05) in the concentration of urea and creatinine in the male rabbit when treated with ethanolic extract of *Petroselinum crispum* at a dose (125 mg/kg) as compared with the positive group, while there was a non-significant difference (p>0.05) of Urea and Creatinine concentration was found in the serum of male rabbits treated with *Petroselinum crispum* at dose (250 mg /kg b.w) and negative control group.

Table 3 effect of *Petroselinum crispum* extract on serum antioxidant enzymes concentration of male rabbits treated with Gentamicin.

Groups	MDA (µmol/l)	SOD (U/ml)	GSH (µmol/l)	CAT (U/ml)	GPX (U)
control group	0.18±0.01 c	106.47±19.23 a	351.00±28.75 a	17.20±2.38 a	109.20±17.25 a
Gentamicin (80mg/kg)	3.29±0.34 a	59.26±20.10 c	157.67±40.35 c	9.08±0.97 c	58.00±0.63 c
Gentamicin (80mg/kg)+PCE(125mg/kg)	1.58±0.40 b	78.53±10.06 b	223.33±25.81 b	11.38±1.62 b	84.16±10.20 b
Gentamicin (80mg/kg)+PCE(250mg/kg)	0.49±0.39 c	97.60± 6.68 a	314.33±15.44 a	17.13±2.09 a	106.38±2.43 a

Different letters mean significant differences (P≤0.05) .

Table 4 effect of *Petroselinum crispum* extract on serum Urea and Creatinine of male rabbits treated with Gentamicin:

Groups	Urea (mg/dL)	Creatinine (mg/dL)
control group	25.83± 1.47 c	0.76 ± 0.10 **c**
Gentamicin (80mg/kg)	439.60 ± 114.13 a	7.75 ± 4.95 a
Gentamicin (80mg/kg)+PCE(125mg/kg)	104.13 ± 15.12 b	4.28 ± 0.84 b
Gentamicin (80mg/kg)+PCE(250mg/kg)	31.21 ± 19.19 c	1.22 ± 0.36 c

Different letters mean significant differences (P≤0.05) .

Effect of gentamicin and ethanolic extract of ***Petroselinum crispum*** **on the morphology of the kidney:**

Morphology examination of kidneys showed normal size , color and form in the control group (Fig.1).while in the kidneys of rabbits treated with gentamicin(80mg / kg), the kidneys appeared pale in colour, bigger in size and

swollen. The kidneys of animals treated with gentamicin were also found to be easily separated from the animal body. (Fig.2). The group that treated with *Petroselinum crispum* at a dose (125 mg /kg B.W) the kidneys are mild pale in colour with enlarged(Fig.3).

In animals treated with *Petroselinum crispum* ethanolic extract at a dosage (250 mg/kg B.W), however, the kidneys retained normal healthy colour and were not easily removed from the animal body. (Fig.4). **Histopathological examination of kidneys:**

rabbits in negative group, the kidney showed normal renal tubules and glomerulus (Figure 5), When Gentamicin was used to induce excessive dilation of renal tubules, proximal tubules are obstruction and atrophy of glomerulus tuff, swelling of epithelial cells, thin capsule (spilt) or any region of wrinkling, dense glomerulus epithelial cells, serious hydropic degeneration, inflammatory cell infiltration in glomerulus lumen, thickening and congested blood vessels, sever cast and proteinaceous material as shown in (Figure 6). Whereas the rabbit kidney was treated with *Petroselinum crispum* ethanolic extract at a dose (125 mg/kg B.W) showed that certain renal tubules are dilatation, dilatation in the medulla, inflammatory cell infiltration (Figure 7). but In (Figure 8) kidney of rabbits that treated with *Petroselinum crispum* at a dose (250 mg /kg B.W) showed renal tubules and glomerulus are normal.

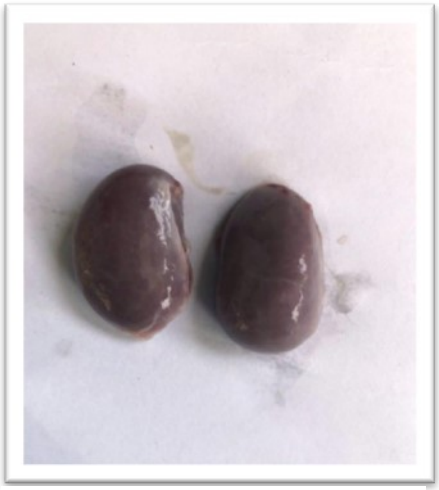

Fig.1: A kidney of control negative rabbit showing bean shape,reddish - Brown in color

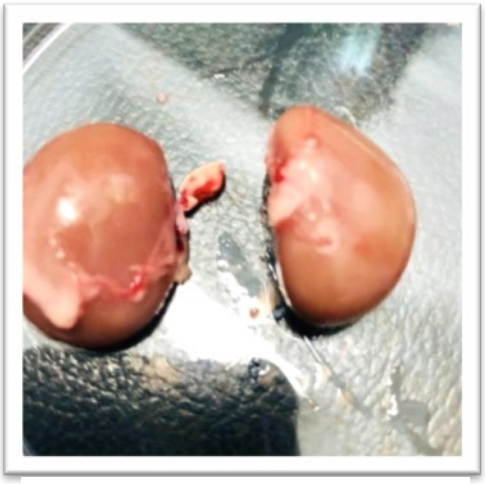

Fig.2: A kidney of conrol positive rabbit showing enlarged,swollen and pale in colour

Fig.3:A kidney of group treated with PCE at dose (125 gm/kg) showing mild pale in colour with enlarged

Fig.4:A kidney of group treated with PCE at dose (250 gm/kg) showing bean shaped ,reddish brown in colour.

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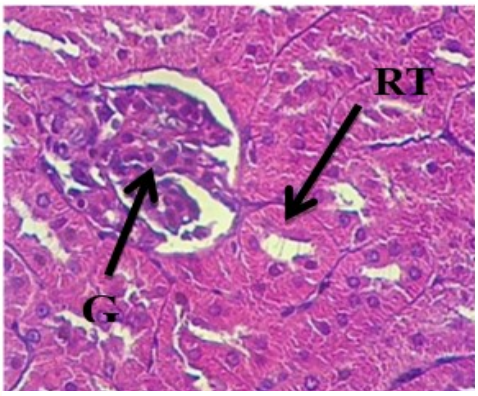

Fig. 5: Histological section of the rabbit kidney of Negative control group showingnormal renal tubule (RT) and glomerulus(G), stained with H&E,(400X)

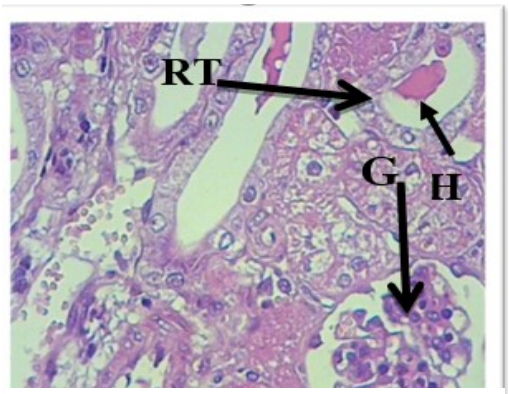

Fig.6: Histological section of the rabbit kidney of positive control group showing dilatation of renal tubule(RT) , infiltration of inflammatory cell, hemorrhage(H) and atrophy in glomerulus(G), stained with H&E,(400X)

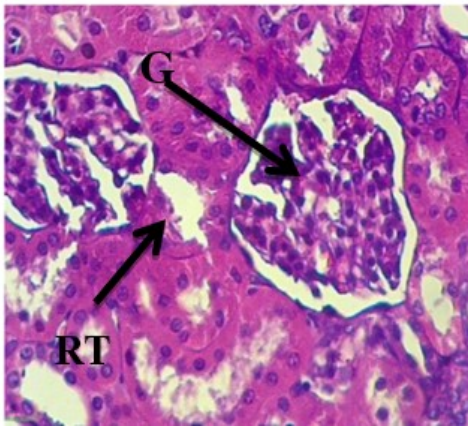

Fig. 7: Histological section of the rabbit kidney of third group showing mild dilatation of renal tubule(RT) , vacuolated of epithelium cells and in glomerulus(G),slight inflammatory cells in interstitial tissue. stained with H&E,(400X)

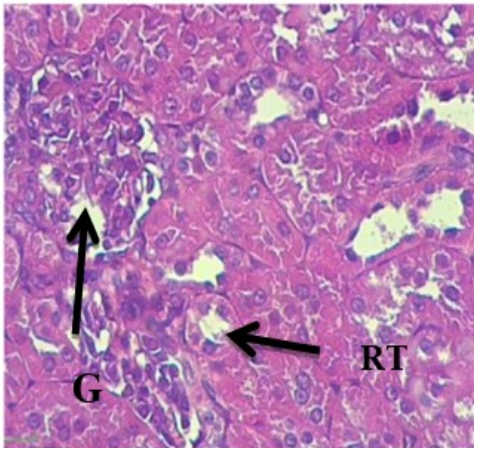

Fig. 8: Histological section of the rabbit kidney of fourth group showing normal renal tubules(RT) and glomerulus tufts(G) , stained with H&E,(400X)

In this study, clinical signs such as lack of appetite, decreased bodyweight, rough and hair loss, hematuria, depression and decreased activity in male rabbits treated with gentamicin was seen at a dosage of 80 mg/kg intramuscular for 15 days, these results agreed with (20). indicated that these clinical signs confirm the severe nephrotoxicity. Gentamicin is primarily produced in the proximal renal tubules because of the cationic property that activates the apoptosis of the negative phospholipid charge. Gentamicin also decreases renal blood flow which has led to the proximal renal tubular damage(21). Nephrotoxic drugs (gentamicin) may cause changes in intraglomerular hemodynamics, glomerular disease, renal vasculitis and thrombosis, tubulointerstitial disease, damage to tubular epithelial cells and obstructive nephropathy(9). In our work, *Petroselinum crispum* ethanolic extract treatment leads to prevent the abnormal signs of toxicity as opposed to the positive control group.

Even male rabbits treated with gentamicin have a significant low in body weight and rise in kidney weight compared to male rabbits treated with *Petroselinum crispum* ethanolic extract treated with gentamicin group. (22) Displayed low body weight may have resulted from aggregation of Gentamicin in the renal tissue, leading to a decline in food intake and bodyweight as a result of renal injury. This condition led the consequent loss of tubular cells to reabsorb water which results in dehydration and weight loss. Our bodyweight results are consistent with previous reports of other researchers who stated that administering gentamicin at a dose level of 80 mg/kg/day for fifteen days produced a statistically significant loss of body weight and kidney increase (20). Enhanced catabolism results in acidosis followed by anorexia, which decreases food intake leading to loss of body weight (23). GM known to cause increased kidney weight and it was due to inflammatory changes and oedema in the proximal tubular epithelial cells (24). While treatment with *P. crispum* ethanolic extract showed a significant rise in final bodyweight and kidney weight reduction in comparison with positive control group may be linked to the fact that the plant is considered to be a good appetite stimulant and to have antioxidant and anti-inflammatory activity through its contents which were flavonoids, proteins, and carbohydrates(25).

There is a significant decline in WBC count, lymphocytes percentage and a significant rise in neutrophil percentage in the group treated with gentamicin and this study is consistent with the (26), The anaemia results from hemodilution of extravascular hemolysis as well as toxic dis-hematopoiesis drugs in this area resulted in decreased WBC values due to cardiovascular depression, resulting in an indicator of GM-induced immune system deficiency. On the other hand, the elevation of neutrophil percentage observed in the present study because the Neutrophils are the first line of defence, versus tissue injury, infectious agents, tissue wounds, bacteria and harmful or toxic substances by phagocytosis (27). Also, The current results have shown that the administration of *Petroselinum crispum* ethanolic extract to gentamicin-intoxicated rabbits normalized the otherwise altered rates of WBC counts as opposed to gentamicin treated group. *P. crispum* is a good source of iron, zinc, Ca and phosphorus (28, 29). And these elements make the *Petroselinum crispum* valuable for food supplements. Zinc curing gentamicin-poisoned animals also raised

the WBC count significantly and improved the total lymphocyte and neutrophil levels. Zinc is essential to protect and defend against harm in the construction of proteins and cell membranes, playing an essential role in immune response growth also development, neurological function and reproduction.(30). *P crispum* also contains n-3 omega fatty acids such as palmitic and linolenic acid may be increased WBC count (31), (32)and (33).

Gentamicin's observed nephrotoxic effect may include oxidative stress because gentamicin adversely affects the parameters of oxidative stress (MDA, SOD, GSH, CAT, and GPX) into the homogeneous kidney tissue(34). The oxidative stress resulting from reactive oxygen generation as a result of nephrotoxicity caused by gentamicin (35); (36). In contrast with the control group in the Gentamicin treatment group, significantly increased levels of MDA, the marker for lipid peroxidation, were observed. Moreover, the high levels of MDA were effectively reduced by ethanolic extract of *P. crispum* treatment, indicating that the composition of reactive oxygen species in Gentamicin mediated nephrotoxicity was scavenged so that the ethanolic extract of *P. crispum* minimized lipid peroxidation(37) and (38).

The reduced GSH, SOD , CAT and GPX activity showed in this study, due to increase in free radicals Gentamicin-induced nephrotoxicity. *P. crispum* treated group significantly improved antioxidant levels in kidneys as compared with control positive group. However, the low in MDA and high in GSH, SOD, CAT and GPX activities when treated with ethanolic extract of *P crispum* could be due to the antioxidant properties of *P crispum*. *P crispum* is rich in poly-phenolic flavonoid anti-oxidants including apiin, apigenin, crisoeriol and luteolin,and has been rated as one of the plant sources with highest anti-oxidant activities(39).

In the our study, drug-induced nephrotoxicity in group of the positive control was characterized by a pronounced rise in the circulating levels of serum urea and serum tubulonephritis creatinine relative to negative control group rabbits. Those research are in agreement (40) and (41). Urea is the primary end product of a catabolism of proteins. Gentamicin injection in general increasing urea and creatinine concentration in the rabbit's blood serum. Enhanced catabolism of proteins and rapid deamination of amino acids for gluconeogenesis is possibly an appropriate postulate for understanding elevated urea. Also, an increase in urea concentration suggested that animals experienced hemoconcentration due to animal dehydration. Significant rise in serum creatinine was also noticed in the group injected with Gentamicin. These results were in accords with (42) Such improvements could be defined as a decrease in glomerular filtration, with a decrease in diuresis. Administering parsley leaves extract with GM substantially reduced serum urea and creatinine in comparison to positive control group.These results coincided with(43) and(44) the using gentamicin-induced nephrotoxicity in rat. using gentamicin-induced nephrotoxicity in rats. The *P crispum* extract mechanism of action appears to be mediated by an suppression of the Na+/K+ pump, which would lead to a decrease in Na+ and K+ re-absorption, leading to osmotic water flows into the lumen and dieresis. The diuretic effect is due to the presence of two ingredients, apiol and myristicin(45).

Due to greater perfusion and precipitation of excreted materials, which occur in renal tubular cells during absorption and secretion, kidneys are readily susceptible to drug damage. GM is a commonly used antibiotic aminoglycoside that has been shown to cause significant histological harm, particularly in renal proximal convoluted tubules. (46), (47) and (48). Extensive and major lesions of the renal system including tubular necrosis and inflammatory cell infiltration (49), shrinkage of the glomeruli, dilated and congested intertubular blood vessels and haemorrhage

within interstitial tissue in cortex and medulla regions associated with leucocytes infiltration. Gentamicin administration to rabbits induced renal function loss by releasing oxygen-free radicals (50).

In the current study, no visible change was observed in kidney histological sections of rabbits treated orally with ethanolic extract of *Petroselinum crispum* (Parsley) of 250 mg/kg b.w with gentamicin in a group as the negative control group. Oral parsley extract treatments in Gentamicin nephrotoxic rabbits led to nephro-protective, diuretic, and antioxidant effects as they opposite biochemical serum parameters also reduced kidney-induced histopathological changes in rabbits. The nephroprotective and diuretic effects of *P. crispum*, reported herein, were similar to those recorded by (51) who found that a polyherbal formulation including *P. crispum* produced nephro-protective and diuretic effects in rat.

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